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ORIGINAL RESEARCH

Appropriate Use Criteria for the Management of Aortic Stenosis

Insight From the Japanese Expert Panel

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ABSTRACT

BACKGROUND The indication for transcatheter aortic valve replacement (TAVR) for aortic stenosis (AS) significantly varies among physicians and institutions.

OBJECTIVES This study aims to develop a set of appropriate use criteria for AS management to assist physicians in decision-making.

METHODS The RAND-modified Delphi panel method was used. A total of >250 common clinical scenarios were identified in terms of whether to perform the intervention for AS and the mode of intervention (surgical aortic valve replacement vs TAVR). Eleven nationally representative expert panelists independently rated the clinical scenario appropriateness on a scale of 1-9, as "appropriate" (7-9), "may be appropriate" (4-6), or "rarely appropriate" (1-3); the median score of the 11 experts was then assigned to an appropriate-use category.

RESULTS The panel identified 3 factors that were associated with a rarely appropriate rating in terms of performing the intervention: 1) limited life expectancy; 2) frailty; and 3) pseudo-severe AS on dobutamine stress echocardiography. Clinical scenarios that were deemed rarely appropriate for TAVR were also identified: 1) patients with low surgical risk and high TAVR procedural risk; 2) patients with coexistent severe primary mitral regurgitation or rheumatic mitral stenosis; and 3) bicuspid aortic valve that was not suitable for TAVR. Importantly, any TAVRs for patients who were older than 75 years of age were not rated as rarely appropriate.

CONCLUSIONS These appropriate use criteria provide a practical guide for physicians regarding clinical situations commonly encountered in daily practice and elucidates scenarios deemed rarely appropriate that are clinical challenges for TAVR. (JACC: Asia 2023;3:255–267) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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JACC: ASIA, VOL. 3, NO. 2, 2023
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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AUC = appropriate use criteria

BAV = bicuspid aortic valve

CABG = coronary artery bypass grafting

DSE = dobutamine stress echocardiography

MR = mitral regurgitation

PCI = percutaneous coronary intervention

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

TEER = transcatheter edge-to-edge repair

Transcatheter aortic valve replacement (TAVR) is recognized as an established therapeutic strategy for treating severe aortic stenosis (AS), regardless of surgical risk.[1,2] The number of procedures has been increasing worldwide. In 2019, approximately 70,000 and 7,000 procedures were performed in the United States and Japan, respectively, and their numbers have exceeded the surgical aortic valve replacement (SAVR) volume.[3,4] However, indications remain variable in many situations encountered in daily practice because of the lack of evidence from large randomized clinical trials, especially those comparing the efficacy and safety of TAVR vs SAVR, regarding factors such as coexistent coronary artery disease, valvular heart disease, bicuspid aortic valve (BAV), and a wide range of clinical patterns that are excluded from randomized clinical trials (eg, patients with dementia, frailty, and dialysis). This raises questions concerning the appropriate indications as well as the overuse or underuse of TAVR.

Appropriate use criteria (AUC) have been developed in various cardiovascular fields to complement clinical practice guidelines.[5-7] AUC scientifically summarizes expert consensus, serving as practical guidance for assessing and better understanding variability in opinions. AUC have been applied in real-world clinical practice, along with various registries, and they identified common clinical scenarios that were deemed as "rarely appropriate" and were the main target of quality improvement.[8,9] In the field of coronary revascularization, AUC have contributed to the standardization of procedural indications and quality of care, leading to quality improvement.[10]

Regarding the management of AS, the American College of Cardiology Foundation and 10 other societies published a joint AUC for the treatment of patients with severe AS in 2017.[11] It was applied in the multicenter TAVR registry, and our group previously reported that the proportion of rarely appropriate TAVRs was approximately 5% with a substantial institutional variation.[12] However, since then, numerous pieces of evidence have emerged, and the guideline-recommended indications for TAVR have been expanded to include patients with a full spectrum of surgical risks.[13] Furthermore, because of the advancement of TAVR technology and technique, the clinical outcome has been much improved.[3] Thus, the AUC must be updated to incorporate the available evidence and reflect current daily clinical practice.

Therefore, nationally represented panel members were selected from various cardiovascular fields and: 1) identified key factors affecting the decision on whether to perform an intervention for AS (either SAVR or TAVR) and key factors affecting the decision on the mode of intervention (SAVR vs TAVR) based on a detailed literature review and interactive discussion; 2) developed >250 clinical scenarios based on the identified key factors; and 3) evaluated the appropriateness of each scenario by scientifically aggregating the opinion of an expert panel using the RAND methodology to provide a framework for the assessment of practice patterns that could facilitate physician decision-making.

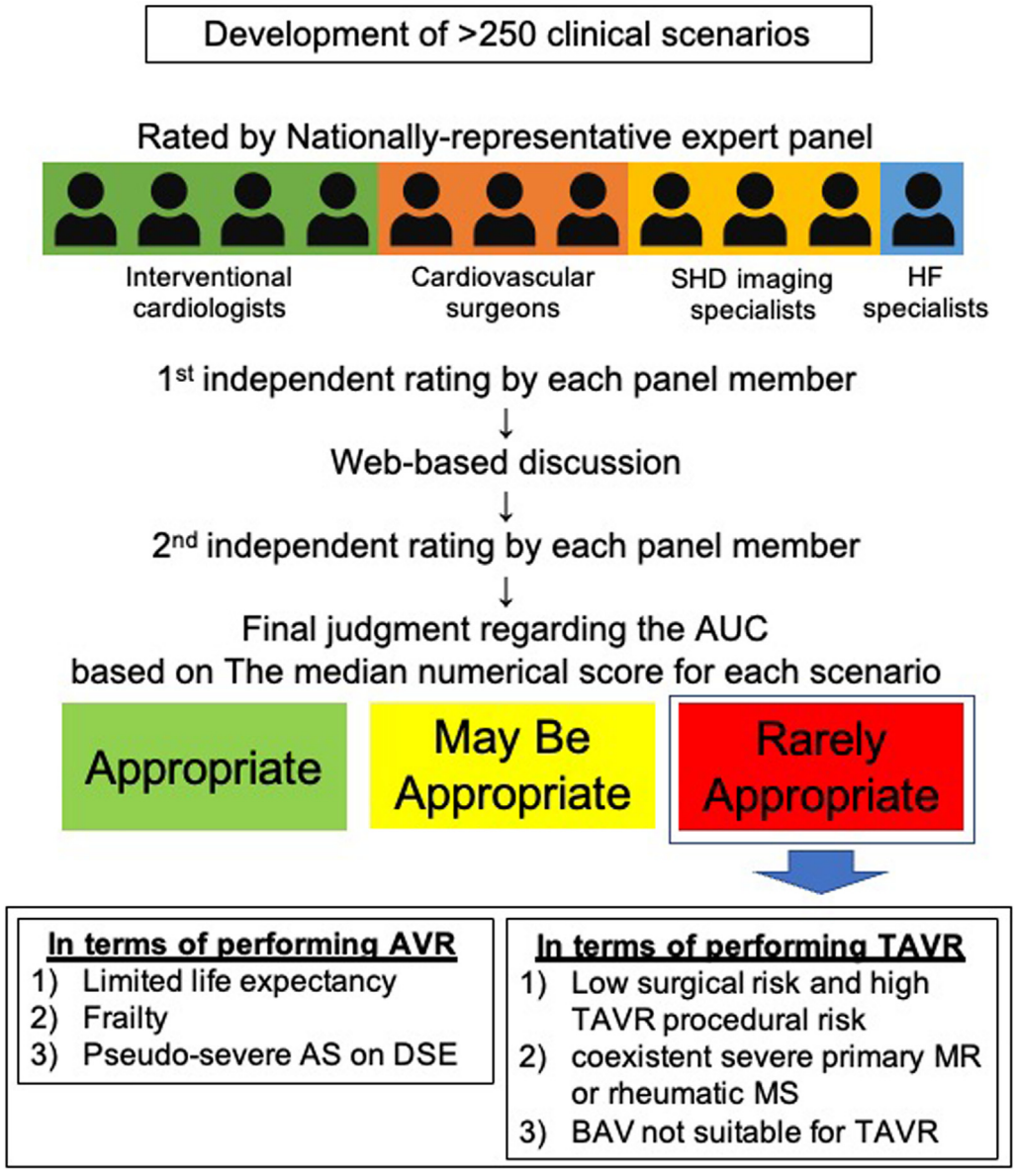
METHODS

Briefly, the RAND methodology in the medical field is a qualitative method used for evaluating the appropriateness of various therapeutic strategies for which sufficient evidence is not available.[14] This method entailed expert panelists who anonymously replied to repeated questionnaires and subsequently received feedback with the best available evidence from interactive discussions with the panelists (the Delphi approach). The purpose of this procedure was to reduce the variety of responses among the panelists and obtain the most reliable conclusions (**Figure 1**).[14,15] An AUC document has 2 main purposes: 1) as a clinical tool, it can assist physicians in better-informing patients on their therapeutic options; and 2) as an administrative and research tool, it can provide a means of comparing patterns of therapeutic strategies among physicians.

PANEL SELECTION. To prevent bias in the scoring process and ensure an appropriate balance of expertise, the expert panel was intentionally made up of expert physicians from various cardiovascular fields. The 11 panelists, including 4 interventional cardiologists, 3 cardiovascular surgeons, 3 structural heart disease imaging specialists, and 1 heart failure specialist, were selected from the OCEAN (Optimized Catheter Valvular Intervention Structural Heart Disease) study.[16] All panelists were asked to state declarations of interest that might be perceived as potential conflicts of interest; these are listed in the acknowledgements section.

DEVELOPMENT OF KEY FACTORS AND CLINICAL SCENARIOS. First, the nonpanel members (2 authors in the present study; Drs Inohara and Otsuka) performed a systematic literature review to identify important topics on AS management encountered in daily practice and key factors that affect the decision-making process for physicians. As a result, >20 key factors and >500 distinct clinical scenarios would be required; however, a level of granularity in this

FIGURE 1 **RAND-Modified Delphi Panel Method**



Using the RAND-modified Delphi panel method, a total of 11 nationally represented panel members developed appropriate ratings for the management of severe aortic stenosis. In the first round, the panelists were asked to independently rate each clinical scenario on a scale of 1-9 using a web-based answer sheet. Then, the panelists participated in an interactive web-based meeting and discussed clinical scenarios for which "disagreement" was confirmed. In the second round, panelists again independently provided their final rating for each clinical scenario through a web-based answer sheet. The median numerical score was calculated for each clinical scenario and then allocated to an appropriate-use category, as follows: median score 7-9 (appropriate care **[green]**), median score 4-6 (may be appropriate care **[yellow]**), and median score 1-3 (rarely appropriate care **[red]**). AUC = appropriate use criteria; AVR = aortic valve replacement; BAV = bicuspid aortic valve; HF = heart failure; MR = mitral regurgitation; MS = mitral stenosis; SHD = structural heart disease; TAVR = transcatheter aortic valve replacement.

JACC: ASIA, VOL. 3, NO. 2, 2023
APRIL 2023:255–267

TABLE 1 Dementia, Frailty, and Life Expectancy[a]

	TAVR / SAVR
Treatment decision with the decision-making support system in patients who have difficulty expressing their own will, such as those with dementia or intubation	7
Treatment decision with the support of the patient's family member	9 (A)
Patients with an anticipated life expectancy of <1 year	3
Patients complicated with cardiomyopathy such as amyloidosis	5
Very frail patients (clinical frailty scale of ≥7)	3

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate."
(A) = "agreement"; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

framework would be troublesome and unlikely to advance the objective of this study. Accordingly, once the key factors and clinical scenarios were drafted by the nonpanel members, the panel members provided feedback, which led to substantial improvements in the selection of key factors and clinical scenarios. Finally, 6 key factors affecting the decision on whether to perform intervention for AS (either SAVR or TAVR) and 8 key factors affecting the decision on the mode of intervention (SAVR vs TAVR) were identified as shown below.

Factors affecting the decision on whether to perform an intervention for AS (either SAVR or TAVR) include: 1) dementia; 2) comorbidities with a life expectancy <1 year; 3) concomitant cardiomyopathy, especially amyloidosis; 4) frailty; 5) asymptomatic severe AS; and 6) low-flow low-gradient AS.

Factors affecting the decision on the mode of intervention (SAVR vs TAVR) include: 1) age; 2) surgical risk; 3) TAVR procedural risk; 4) concomitant coronary artery disease requiring revascularization; 5) concomitant valvular disease; 6) BAV; 7) degenerative surgical bioprosthesis; and 8) noncardiac surgery.

Each guideline has proposed its age threshold for determining the mode of intervention (SAVR vs TAVR). In the European guidelines, the age of 75 years is the threshold to determine the mode of interventional (SAVR vs transfemoral TAVR [TF-TAVR]).[2] In the U.S. guidelines, there is a wide gray zone, and for patients aged 65 to 80 years, either SAVR or TF-TAVR is recommended.[1] Similar to the E.U. guidelines, the Japanese guidelines recommend SAVR for patients who are <75 years of age. However, either SAVR or TF-TAVR is recommended for patients who are 75 to 80 years of age, and TF-TAVR is recommended for those who are >80 years of age.[13] Given that TAVR has been expanding its indication toward the younger population, the panelists determined to set the age of 75 years as a threshold for generating clinical scenarios, despite the presence of a gray zone (ages ranging from 75 to 80 years) in the Japanese guidelines.

The surgical risk was traditionally determined by the Society of Thoracic Surgeons (STS) risk score. However, to determine the mode of intervention (SAVR or TAVR), factors that are not included in the STS risk score, such as a porcelain aorta, chest deformation, or interstitial pneumonia, should be considered. In our clinical scenarios, "surgical risk" indicated risks accounting for factors that are not represented by the STS risk score. TAVR procedure risks were the factors that may increase the risk of the TF-TAVR procedure, such as bulky calcification of the left ventricular outflow tract, shaggy aorta, or unfavorable vascular access.

RATING PROCESS. **First rating: no interaction.** In the first round, the panelists were asked to independently rate each clinical scenario on a scale of 1-9, using a web-based answer sheet. The panelists were asked to recognize the variability in various patient factors, local practice trends, and a lack of evidence regarding the intervention for AS in all possible clinical scenarios. The intervention was considered appropriate when the potential benefits, in terms of survival or health outcomes (symptoms, functional status, and/or quality of life), outweighed the potential negative consequences of the intervention.[14] Scores of 7-9 indicated that the management was considered "appropriate" for the clinical scenario presented. Scores of 1-3 indicated that the intervention was considered "rarely appropriate" for the clinical scenario, whereas scores in the mid-range (4-6) indicated that the intervention "may be appropriate" for the clinical scenario.

Second rating: after a web-based discussion in a web meeting. In the second round, which took place in the form of a web meeting on April 18, 2022, the panelists participated in an interactive web-based meeting. At the meeting, the best available evidence regarding each scenario was provided to the expert panel. After confirming the general assumptions and points of confusion, the panelists discussed clinical scenarios for which disagreement was confirmed at the first rating. Then, panelists again independently provided their final rating for each clinical scenario through a web-based answer sheet.

AGGREGATION AND FINAL JUDGMENT OF APPROPRIATENESS. When generating the final results, each panelist's rating had equal weight, and the

consensus was not coerced. The median numerical score was calculated for each clinical scenario and then allocated to an appropriate-use category as follows: median score 7-9 (appropriate care [shown in green on accompanying tables]), median score 4-6 (may be appropriate care [shown in yellow on accompanying tables]), and median score 1-3 (rarely appropriate care [shown in red on accompanying tables]).

RATING AGREEMENT. The primary objective of the present report was to provide a tool for assessing the appropriateness of the intervention for AS in various clinical scenarios. The consensus among ratings was desirable, but achieving complete consensus among the diverse panelists would have been arbitrary and contrary to the aim of the process.

The agreement was left unquestioned in the final assessment of appropriateness; however, information regarding agreement/disagreement was provided to guide the round-table interactive discussion, emphasizing the panelists' areas of difference. It was also used to assess whether the 2 rounds of ratings, with a substantial discussion between the ratings, led to some consensus among the panelists.

The degree of agreement between panelists, as described by RAND, was evaluated for each clinical scenario. "Agreement" among the panelists was defined as the condition in which the ratings of at most 2 panelists fell outside the range of the 3 points containing the median score; "disagreement" was defined as the condition in which the ratings of at least four panelists fell in both appropriate and inappropriate categories. Based on these definitions, some clinical scenarios were classified into "neither agreement nor disagreement."

GENERAL ASSUMPTIONS. The comments and scenarios in this document were limited to patients with severe AS and were not intended to be applied to those with mild or moderate disease. Diagnostic tests and procedures were performed and interpreted by qualified individuals in a facility that complied with national standards for performing echocardiography, computed tomography, coronary angiography, invasive hemodynamic assessment, interventions such as SAVR and TAVR, and other transcatheter and surgical procedures. TAVR indicated TF-TAVR, and alternative approaches, such as transapical, transubclavian, or transaortic approach, were not included. For some clinical scenarios, more than 1 table was consulted to determine the appropriateness of a specific intervention. For example, an applicable scenario in Table 1 may have indicated that intervention (SAVR or TAVR) was appropriate. An additional table, such as Table 2, which included information on surgical risk and comorbidities, may have needed to be consulted to determine the appropriateness of SAVR or TAVR specifically.

TABLE 2 Asymptomatic Severe AS[a]

	TAVR / SAVR
SAVR for patients with severe AS and other indications for open heart surgery	9 (A)
Severe AS with reduced LVEF (<50%)	8 (A)
Severe AS **with** any of the criteria shown below • Symptoms or significant drop in blood pressure during stress test • Concomitant significant pulmonary hypertension AS (systolic pulmonary artery pressure of ≥60 mm Hg) • Rapid AS progression (delta Vmax >0.3 m/s/y)	8 (A)
Severe AS **without** any of the criteria shown below • Symptoms or significant drop in blood pressure during stress test • Concomitant significant pulmonary hypertension AS (systolic pulmonary artery pressure ≥60 mm Hg) • Rapid AS progression (delta Vmax >0.3 m/s/year) • Reduce LVEF (<50%)	5
Elevated BNP in severe AS with preserved LVEF	5
Leg edema in severe AS with preserved LVEF	4
Very severe AS (Vmax >0.3 m/s ≥5 m/s, mean pressure gradient ≥60 mm Hg, or AVA<0.6 cm^2)	9 (A)

[a]Green represents "appropriate," yellow represents "may be appropriate."

AS = aortic stenosis; AVA = aortic valve area; BNP = B-type natriuretic peptide; LVEF = left ventricular ejection fraction; other abbreviations as in Table 1.

TABLE 3 Low Gradient AS[a]

	TAVR / SAVR Symptom	
	-	+
Reduced EF low-flow low-gradient AS (AVA ≤1.0 cm^2 [or iAVA ≤0.6 cm^2/m^2] on resting echo LVEF <50% Low-flow low-gradient)		
Flow reserve on low-dose dobutamine echo (DSE) Truly severe AS	6	9 (A)
Flow reserve on DSE Pseudo-severe AS	3 (A)	5
No flow reserve on DSE Very calcified aortic valve (high Ca score)	5 (A)	7 (A)
No flow reserve on DSE No apparent calcified aortic valve (low Ca score)	2 (A)	4
DSE not performed Very calcified aortic valve (high Ca score)	5	7 (A)
DSE not performed No apparent calcified aortic valve (low Ca score)	2 (A)	4
Preserved EF low-gradient AS (AVA ≤1.0 cm^2 [or iAVA ≤0.6 cm^2/m^2] on resting echo LVEF ≥50%)		
Low-flow low-gradient Very calcified aortic valve (high Ca score)	5	8 (A)
Low-flow low-gradient No apparent calcified aortic valve (low Ca score)	3	5
Normal-flow low-gradient Very calcified aortic valve (high Ca score)	4	7
Normal-flow low-gradient No apparent calcified aortic valve (low Ca score)	2 (A)	4

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate."

DSE = dobutamine stress echocardiography; iAVA = indexed aortic valve area; other abbreviations as in Tables 1 and 2.

JACC: ASIA, VOL. 3, NO. 2, 2023
APRIL 2023:255–267

TABLE 4 Patients With Severe AS and Various Comorbidities[a]

	SAVR		TAVR	
Symptomatic Severe AS	**<75 y**	**≥75 y**	**<75 y**	**≥75 y**
Nondialysis patients with sufficient anticipated life expectancy				
Surgical risk: high TAVR procedural risk: low	3	2 (A)	8 (A)	9 (A)
Surgical risk: low TAVR procedural risk: high	9 (A)	8 (A)	2 (A)	4
Surgical risk: high TAVR procedural risk: high	5	4	5 (A)	7
Surgical risk: low TAVR procedural risk: low	9 (A)	7	5	9 (A)
Dialysis patients with sufficient anticipated life expectancy				
Surgical risk: high TAVR procedural risk: low	3 (A)	1 (A)	8 (A)	9 (A)
Surgical risk: low TAVR procedural risk: high	9 (A)	7	2	5
Surgical risk: high TAVR procedural risk: high	5	2 (A)	5	7
Surgical risk: low TAVR procedural risk: low	9 (A)	7	5	8 (A)
Patients with comorbidities that affect life expectancy (but anticipated life expectancy >1 y)				
Surgical risk: high TAVR procedural risk: low	3 (A)	1 (A)	9 (A)	9 (A)
Surgical risk: low TAVR procedural risk: high	8 (A)	7	3	5
Surgical risk: high TAVR procedural risk: high	4	3 (A)	6	8 (A)
Surgical risk: low TAVR procedural risk: low	7 (A)	5	8 (A)	9 (A)

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate. Abbreviations as in Tables 1 and 2.

We did not obtain ethical/institutional review board approval for the present study because no patient data was required for the analysis.

RESULTS

A total of 264 clinical scenarios were rated. Among them, an agreement was obtained in a total of 122 clinical scenarios (46.2%). There was no clinical scenario that resulted in a disagreement. The remaining clinical scenarios (53.8%) were categorized into "neither agreement nor disagreement."

WHETHER TO PERFORM AN INTERVENTION FOR AS (EITHER SAVR OR TAVR).

Tables 1 to 3 were designed to highlight decision-making on whether to perform an intervention (either SAVR or TAVR) in various clinical settings.

Dementia, frailty, and life-expectancy. In Table 1, patients with an anticipated life expectancy of <1 year and exceedingly frail patients were considered "rarely appropriate." Conversely, for patients who have difficulty expressing their own will, such as those with dementia, the decision to perform an intervention was considered "appropriate" if it was made with the decision-making support system.

Asymptomatic severe aortic stenosis. Table 2 was designed to highlight decision-making in patients with asymptomatic severe AS. Even for asymptomatic patients, any signs of disease progression, such as reduced left ventricular ejection fraction (LVEF), symptoms or significant drop in blood pressure during exercise testing, significant pulmonary hypertension, or rapid AS progression, justify the intervention for AS (appropriate). However, the intervention for patients without any of the above-mentioned signs may not be allowed (may be appropriate).

Low-gradient AS. Table 3 focuses on low-gradient AS with reduced LVEF or preserved LVEF. In patients with reduced LVEF, the interpretation of dobutamine stress echocardiography (DSE) was the key to determining the appropriate ratings. If DSE showed pseudo-severe AS, the clinical scenario was deemed to be "rarely appropriate." If DSE showed no flow reserve or DSE was not performed, the appropriate ratings differed according to the degree of a calcified aortic valve on computed tomography. The clinical scenarios were considered to be rarely appropriate for patients without a very calcified aortic valve, whereas they may be appropriate for patients with a very calcified aortic valve. Regardless of LVEF, patients with any symptoms were likely to be classified into a more appropriate category than asymptomatic patients.

THE MODE OF INTERVENTION (SAVR VS TAVR).

Tables 4 to 8 were designed to highlight decision-making on the mode of intervention (SAVR vs TAVR) in various clinical settings.

Various comorbidities. Table 4 focuses on clinical scenarios with the comorbidities with sufficient life expectancy in nondialysis patients, comorbidities with sufficient life expectancy in dialysis patients, and comorbidities with a limited life expectancy. The expert panel was likely to rate rarely appropriate or may be appropriate for TAVR in clinical scenarios with a high TAVR procedural risk; this trend was more prominent in patients <75 years of age. Conversely, clinical scenarios with high surgical risk were likely to be rated as rarely appropriate or may be appropriate for SAVR, regardless of their TAVR procedural risks, and this trend was more prominent in patients >75 years of age.

Concomitant coronary artery disease requiring revascularization. Management of patients with severe symptomatic AS with coexistent stable coronary artery disease requiring revascularization is summarized in Table 5. In these clinical scenarios, the coronary stenotic lesion was classified into 2 categories: coronary artery bypass grafting (CABG) favor anatomy vs percutaneous coronary intervention (PCI) favor anatomy. The judgment (CABG favor anatomy vs PCI favor anatomy) was determined by the agreement of the heart team, not solely based on the SYNTAX score. The SAVR plus CABG strategy was likely to be rated as rarely appropriate in the clinical scenarios with a high surgical risk and PCI favor anatomy, regardless of LVEF, and the trend was more prominent in patients >75 years of age. However, the TAVR plus PCI strategy was rated as may be appropriate in the clinical scenarios with either TAVR procedural high risk or CABG favor anatomy, and the trend was more prominent in patients <75 years of age. Particularly younger patients (<75 years of age) with the combination of low surgical risk, TAVR procedural high risk, and CABG favor anatomy were rated as rarely appropriate for TAVR plus PCI.

Concomitant other valvular heart disease. Table 6 was constructed using common clinical scenarios of other valvular and structural heart conditions that are commonly encountered when treating patients with severe AS. Patients with concomitant severe primary mitral regurgitation (MR) were likely to be deemed as appropriate for surgical approach (SAVR plus mitral valvuloplasty or replacement), whereas those with concomitant secondary MR were likely to be deemed as appropriate for TAVR. For clinical scenarios with concomitant severe mitral valve stenosis, regardless of its etiology (rheumatic mitral valve stenosis vs mitral annulus calcification mitral valve stenosis), the panel rated them as appropriate for surgical approach in patients with low surgical risk and may be appropriate or rarely appropriate in those with high surgical risk.

Severe AS due to BAV. Table 7 addresses the clinical situation in patients with severe AS due to BAV. BAV was classified into 2 categories (TAVR favorable vs TAVR unfavorable) according to the previous literature; BAV with calcified raphe and excess leaflet calcification was considered as TAVR unfavorable.[17] Patients with a dilated ascending aorta (≥4.5 cm) were likely to be rated as appropriate for the surgical approach, whereas TAVR was not considered may be appropriate or rarely appropriate for these patients. In patients without a dilated ascending aorta, BAV anatomy was the key factor to determine the appropriate ratings. The panel rated as appropriate for TAVR in patients with TAVR favorable BAV, whereas those with TAVR unfavorable BAV were deemed as may be appropriate or rarely appropriate for TAVR.

TABLE 5 Patients With Severe AS and Concomitant Coronary Artery Disease Requiring Revascularization[a]

Symptomatic Severe AS	SAVR+CABG		TAVR+PCI	
	<75 y	≥75 y	<75 y	≥75 y
Preserved LVEF (≥50%)				
Coronary stenotic lesion: PCI favor Surgical risk: high TAVR procedural risk: low	3	1 (A)	8 (A)	9 (A)
Coronary stenotic lesion: CABG favor Surgical risk: high TAVR procedural risk: low	7	4	6 (A)	7 (A)
Coronary stenotic lesion: PCI favor Surgical risk: low TAVR procedural risk: high	8 (A)	7	4 (A)	6 (A)
Coronary stenotic lesion: CABG favor Surgical risk: low TAVR procedural risk: high	9 (A)	9 (A)	3 (A)	4
Coronary stenotic lesion: PCI favor Surgical risk: high TAVR procedural risk: high	5	3 (A)	6 (A)	7 (A)
Coronary stenotic lesion: CABG favor Surgical risk: high TAVR procedural risk: high	7	5 (A)	4 (A)	5 (A)
Coronary stenotic lesion: PCI favor Surgical risk: low TAVR procedural risk: low	8 (A)	5	7	9 (A)
Coronary stenotic lesion: CABG favor Surgical risk: low TAVR procedural risk: low	9 (A)	8 (A)	4	7 (A)
Reduced LVEF (<50%)				
Coronary stenotic lesion: PCI favor Surgical risk: high TAVR procedural risk: low	4	1 (A)	8 (A)	9 (A)
Coronary stenotic lesion: CABG favor Surgical risk: high TAVR procedural risk: low	6	4	6 (A)	8 (A)
Coronary stenotic lesion: PCI favor Surgical risk: low TAVR procedural risk: high	9 (A)	7	5	7
Coronary stenotic lesion: CABG favor Surgical risk: low TAVR procedural risk: high	9 (A)	7 (A)	5	6
Coronary stenotic lesion: PCI favor Surgical risk: high TAVR procedural risk: high	3 (A)	2 (A)	6 (A)	7 (A)
Coronary stenotic lesion: CABG favor Surgical risk: high TAVR procedural risk: high	5 (A)	4	5	6
Coronary stenotic lesion: PCI favor Surgical risk: low TAVR procedural risk: low	8	5	8	9 (A)
Coronary stenotic lesion: CABG favor Surgical risk: low TAVR procedural risk: low	9 (A)	7	5	7 (A)

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate."

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; other abbreviations as in Tables 1 and 2.

JACC: ASIA, VOL. 3, NO. 2, 2023
APRIL 2023:255–267

TABLE 6 Patients With Severe AS and Concomitant Other Valvular Heart Disease[a]

Symptomatic Severe AS	SAVR + Other Valve Surgery		TAVR	
	<75 y	≥75 y	<75 y	≥75 y
Severe primary mitral regurgitation Surgical risk: high	7	5	6	8 (A)
Severe primary mitral regurgitation Surgical risk: low	9 (A)	8 (A)	2 (A)	4
Severe secondary mitral regurgitation Surgical risk: high	4	2 (A)	7 (A)	9 (A)
Severe secondary mitral regurgitation Surgical risk: low	8 (A)	5	5	8 (A)
Severe rheumatic mitral stenosis Surgical risk: high	6 (A)	4	7	8 (A)
Severe rheumatic mitral stenosis Surgical risk: low	9 (A)	8 (A)	2	5
Severe MAC mitral stenosis Surgical risk: high	4	2 (A)	7 (A)	8 (A)
Severe MAC mitral stenosis Surgical risk: low	8 (A)	7	5	6
Severe tricuspid regurgitation Surgical risk: high	6 (A)	4	7 (A)	8 (A)
Severe tricuspid regurgitation Surgical risk: low	9	8	4	7

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate. MAC = mitral annular calcification; other abbreviations as in Tables 1 and 2.

Degenerative surgical bioprosthesis. Table 8 summarizes the appropriate ratings of interventions in patients who were symptomatic because of a failing aortic bioprosthesis. In patients >75 years of age, TAVR (transcatheter aortic valve implantation within failed bioprosthetic surgical aortic valves) was judged to be appropriate, regardless of surgical risk and TAVR procedural risk, whereas it was deemed to may be appropriate in patients <75 years of age. Redo SAVR was rated as rarely appropriate in patients with both high surgical risk and low TAVR procedural risk regardless of the patient's age, and the ratings were consistent regardless of the size of the degenerative surgical bioprosthesis.

TABLE 7 Severe AS Due to Bicuspid Aortic Valve[a]

Symptomatic Severe AS	SAVR		TAVR	
	<75 y	≥75 y	<75 y	≥75 y
Bicuspid aortic valve: TAVR favorable Ascending aorta <4.5 cm Surgical risk: high	5	2 (A)	7 (A)	9 (A)
Bicuspid aortic valve: TAVR favorable Ascending aorta <4.5 cm Surgical risk: low	8 (A)	6	5	8 (A)
Bicuspid aortic valve: TAVR unfavorable Ascending aorta <4.5 cm Surgical risk: high	7 (A)	5	4	6
Bicuspid aortic valve: TAVR unfavorable Ascending aorta <4.5 cm Surgical risk: low	9 (A)	8 (A)	2 (A)	4
Bicuspid aortic valve: TAVR favorable Ascending aorta ≥4.5 cm Surgical risk: high	6	4	6	8 (A)
Bicuspid aortic valve: TAVR favorable Ascending aorta ≥4.5 cm Surgical risk: low	9 (A)	7 (A)	4	7
Bicuspid aortic valve: TAVR unfavorable Ascending aorta ≥4.5 cm Surgical risk: high	8 (A)	5 (A)	3	5
Bicuspid aortic valve: TAVR unfavorable Ascending aorta ≥4.5cm Surgical risk: low	9 (A)	9 (A)	2 (A)	4

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate. Abbreviations as in Tables 1 and 2.

Major noncardiac surgery in patients with severe AS. Clinical scenarios in Table 9 deal with the need for major noncardiac surgery in patients with severe AS. The rating panel addressed the appropriateness of intervention on the aortic valve to reduce the risk of major noncardiac surgery. The pivotal issues under consideration were: 1) whether the major noncardiac surgery was elective or urgent; and 2) whether the severe AS was symptomatic or asymptomatic. The rating panel determined it appropriate to perform TAVR before noncardiac surgery regardless of its urgency and patient symptoms. On the contrary, performing SAVR before noncardiac surgery was relatively less appropriate, especially in patients with asymptomatic severe AS who were undergoing urgent noncardiac surgery.

DISCUSSION

Using the RAND-modified Delphi panel method, a total of 11 nationally represented panel members developed appropriate ratings for the management of severe AS (Central Illustration). The ratings consisted of 2 steps: 1) to evaluate whether the decision to perform a valve replacement, either SAVR or TAVR, was appropriate; and 2) to evaluate the appropriateness of the mode of intervention (SAVR vs TAVR). The panel identified 3 factors that were associated with rarely appropriate ratings in terms of performing the intervention: life expectancy of <1 year, too frail, and pseudo-severe AS on DSE or low-gradient AS that was not evaluated by DSE. Clinical scenarios that were deemed rarely appropriate for TAVR were also identified. Importantly, any TAVRs for patients who were >75 years of age were not rated rarely appropriate. Typical clinical scenarios that were rated rarely appropriate were as follows: 1) patients with low surgical risk and high TAVR procedural risk, especially those who had concomitant coronary artery disease that was suitable for CABG; 2) patients with coexistent severe primary MR or severe rheumatic mitral valve stenosis; and 3) patients with severe AS due to BAV that was not suitable for TAVR. The present report represents the current understanding of

AS management and may help to standardize and advance the quality of care, thereby improving patient outcomes.

The decision to perform the intervention should be made in situations where its benefits outweigh its potential risks. In this regard, patients who have a comorbidity that may limit their life expectancy, or who are too frail are considered not to be good candidates for intervention. Shimura et al[18] reported from the OCEAN-TAVR registry that the Clinical Frailty Scale, a semiquantitative tool to assess patients' frailties, was a useful marker for predicting late mortality, and a Clinical Frailty Scale value of ≥7 was associated with poor outcomes; therefore, a Clinical Frailty Scale of ≥7 was used as a cutoff value in the clinical scenarios. Whether to perform the intervention for patients with dementia is a clinical dilemma. Patients with dementia may not adequately describe their symptoms and express their wishes for intervention. To presume patient intent and help patients make the best decision, the decision-making support system including the patient's family members is warranted. In this study, to promote the importance of the decision-making support system to the caregivers, the panel rated the decision to perform the intervention for patients with dementia as appropriate as far as the system was well functioning.

To provide the benefit that is commensurate with the procedural risk, low-dose DSE to distinguish true classical low-flow, low-gradient severe AS from pseudo-severe AS is recommended in the clinical guidelines.[1,2] To reflect these guideline recommendations, the panel rated it rarely appropriate for clinical scenarios in which DSE showed pseudo-severe AS or DSE was not performed. Kataoka et al[19] showed that only 22% of eligible patients with low-flow low-gradient AS underwent DSE before TAVR. Therefore, the implementation of DSE should be encouraged to improve proper patient selection. Importantly, for symptomatic patients, even when DSE showed pseudo-severe AS or DSE was not performed, the panel provided more appropriate ratings and rated it may be appropriate for performing the intervention. Calcium scoring by computed tomography can be very useful to assess the severity of AS in patients with low-flow, low-gradient AS, and confirming severe AS is recommended in U.S. and European guidelines.[1,2] Based on the recommendations, the intervention was likely to be rated as more appropriate in low-gradient AS patients with a very calcified aortic valve compared with no apparent calcified aortic valve.

TABLE 8 Degenerative Surgical Bioprosthesis[a]

	Redo SAVR		TAV in SAV	
Symptomatic severe AS or AR	**<75 y**	**≥75 y**	**<75 y**	**≥75 y**
Degenerative surgical bioprosthesis - size ≤19 mm				
Surgical risk: high TAVR procedural risk: low	3	2	8 (A)	9 (A)
Surgical risk: low TAVR procedural risk: low: high	9 (A)	7	4	5
Surgical risk: high TAVR procedural risk: low: high	5 (A)	4	6 (A)	7 (A)
Surgical risk: low TAVR procedural risk: low: low	8 (A)	7	5	8 (A)
Degenerative surgical bioprosthesis - size >19 mm				
Surgical risk: high TAVR procedural risk: low: low	3	2 (A)	8 (A)	9 (A)
Surgical risk: low TAVR procedural risk: low: high	9 (A)	7	4	7
Surgical risk: high TAVR procedural risk: low: high	5	4	6	7
Surgical risk: low TAVR procedural risk: low: low	8 (A)	7	6	9 (A)

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate."

TAV in SAV = transcatheter aortic valve implantation within failing surgical aortic bioprostheses; other abbreviations as in Table 1.

Estimated surgical risks, traditionally represented by the STS risk score, can aid in determining the mode of intervention; however, several studies have shown the limits of current scoring systems to properly evaluate the procedural risk of TAVR.[20] In addition, several factors are not included in these scoring systems, such as anatomical factors (porcelain aorta, chest deformation, shaggy aorta, narrow sinotubular junction, or calcification on left ventricular outflow tract), interstitial pneumonia, or frailty, but have a

TABLE 9 Major Noncardiac Surgery in Patients With Severe AS[a]

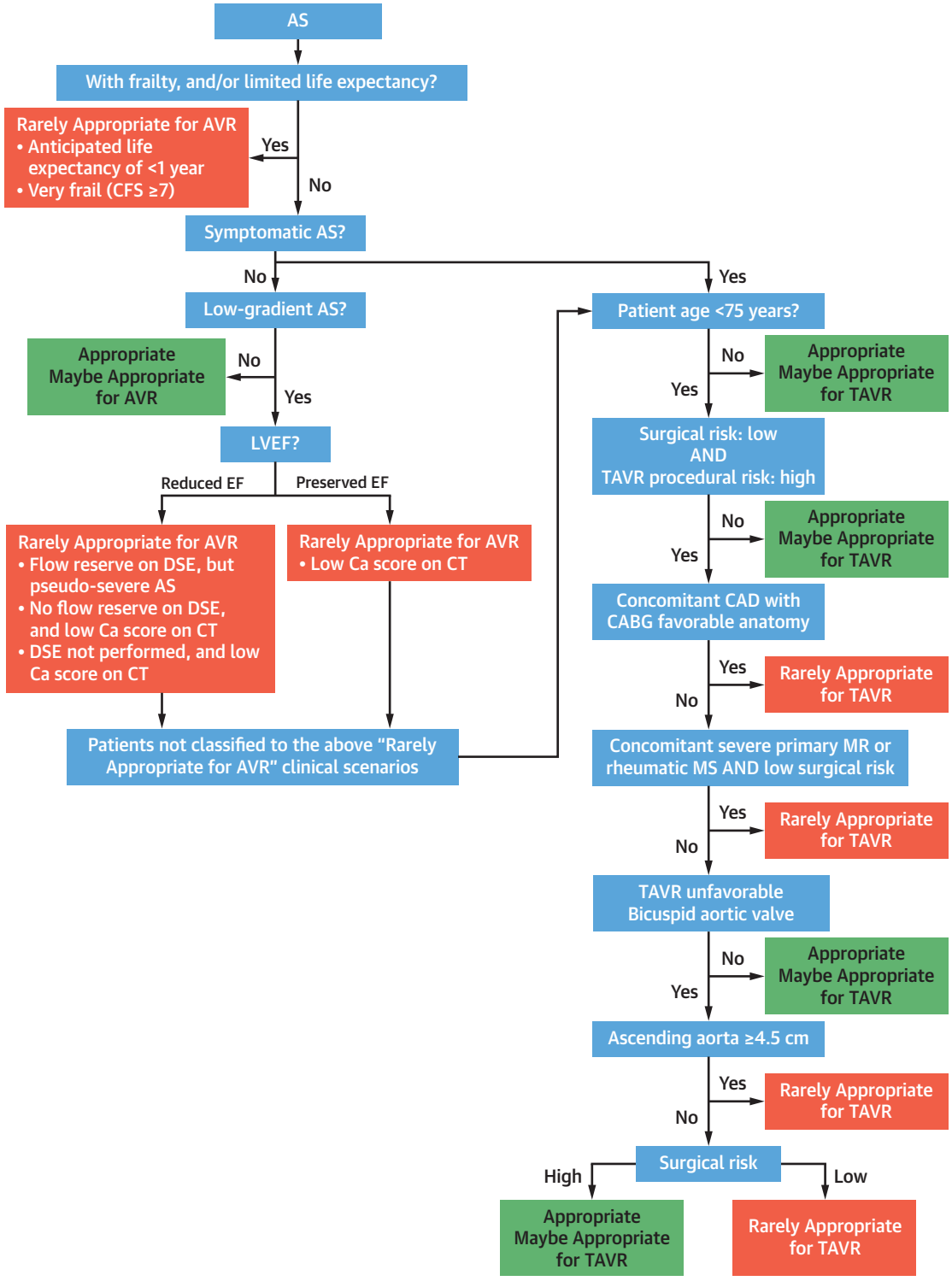
	SAVR		TAVR	
	<75 y	**≥75 y**	**<75 y**	**≥75 y**
Symptomatic severe AS Elective major surgery Nonobstructive CAD	7	5	7	9 (A)
Symptomatic severe AS Urgent major surgery Nonobstructive CAD	5	4	7 (A)	9 (A)
Asymptomatic severe/critical AS Elective major surgery Nonobstructive CAD	5 (A)	4	6	7 (A)
Asymptomatic severe/critical AS Urgent major surgery Nonobstructive CAD	3	3	7	8

[a]Green represents "appropriate," yellow represents "may be appropriate," and red represents "rarely appropriate."

CAD = coronary artery disease; other abbreviations as in Table 1.

JACC: ASIA, VOL. 3, NO. 2, 2023
APRIL 2023:255–267

CENTRAL ILLUSTRATION Decision Tree



Inohara T, et al. JACC: Asia. 2023;3(2):255–267.

Continued on the next page

significant impact on the decision-making process. Given that, the risks for SAVR or TAVR should be judged on a case-by-case basis; therefore, we decided to avoid the use of uniform indicators, such as STS risk score, in clinical scenarios with comorbidities. The heart team discussion was mandatory to accurately estimate surgical and TAVR procedural risks, leading to the best therapeutic strategy.

The etiology of concomitant MR differentiated the appropriate ratings. TAVR for patients with concomitant secondary MR was likely to be rated as "Appropriate", whereas TAVR for those with coexistent primary MR was rated as less appropriate. In these clinical scenarios, if TAVR is chosen for treating severe AS, residual MR would also be treated using the transcatheter approach (ie, transcatheter edge-to-edge repair [TEER]). Therefore, the difference in appropriate ratings between MR etiologies reflects the appropriateness of TEER for primary MR vs secondary MR. The efficacy and safety of TEER for the treatment of MR are well recognized, regardless of its etiology.[21,22] However, more rapid growth in the number of patients undergoing TEER is expected for secondary MR, as surgery is not frequently performed in patients with isolated secondary MR[23-25]; the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) trial documented the superiority of TEER compared with medical therapy alone.[22] The combined transcatheter approach, such as TAVR plus TEER, could provide a new therapeutic option and affect the appropriate ratings.

Because of the advancement in TAVR technology and technique, the outcome of TAVR for BAV has improved significantly; however, the rate of adverse events in patients with BAV has remained slightly higher than that in tricuspid aortic valve patients with a higher rate of equal or greater than moderate perivalvular regurgitation and a lower rate of device success.[26] Yoon et al[17] showed that outcomes of TAVR in BAV depend on valve morphology; calcified raphe and excess leaflet calcification were associated with increased risk of procedural complications and midterm mortality. Reflecting these recent findings, the panel rated younger patients with BAV and unfavorable anatomy rarely appropriate for TAVR. Further trials are needed to define the anatomic features of BAV that are the most suitable for TAVR, the optimal sizing technique, and the best implantation techniques.

The 2017 U.S.-derived AUC must be adapted to the current practice in the Asian AS population for various reasons. First, numerous pieces of evidence have emerged since the AUC development, and the guideline-recommended indications of TAVR have been widely expanded. Second, there are substantial interracial differences in clinical, anatomic, and procedural characteristics in TAVR patients.[27] The Asian population, particularly the Japanese population, is recognized to have a generally longer average life expectancy than the Western population. In addition, the small aortic size and peripheral vessels in Asian patients are of significant concern to physicians because of the potential increased risk for complications. Furthermore, several reports have shown that the proportion of BAV is higher in the Asian population, especially in the Chinese population, compared with that in the Western population.[28] These racial differences may affect the decision on whether to perform an intervention for AS or the decision on the mode of intervention and must be accounted for in the AUC. We believe our newly updated AUC could help facilitate the heart team discussion and lead to the improvement in patient outcomes.

STUDY LIMITATIONS. Our findings should be interpreted in the context of several limitations and considerations. First, the expert panel consisted of nationally representative members; however, it only included Japanese physicians. Therefore, although currently available evidence was considered, the

CENTRAL ILLUSTRATION Continued

Using the RAND-modified Delphi panel method, a total of 11 nationally represented panel members developed appropriate ratings for the management of severe aortic stenosis (AS). Appropriate ratings were classified into 3 categories: appropriate, maybe appropriate, and rarely appropriate. The ratings consisted of 2 steps: 1) to evaluate whether the decision to perform a valve replacement, either surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR), was appropriate **(left side)**; and 2) to evaluate the appropriateness of the mode of intervention (SAVR vs TAVR) **(right side)**. In this decision tree, only clinical scenarios that could be potentially rated as "rarely appropriate" for TAVR are focused and some important factors affecting the decision are not mentioned. Importantly, this decision tree is a decision-aid tool and appropriateness could be changed by various factors and should be evaluated on a case-by-case basis. AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CFS = clinical frail scale; CT = computed tomography; DSE = dobutamine stress echocardiography; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; MS = mitral stenosis.

appropriateness was rated based on Japanese practical guidelines and daily practice in Japan. Furthermore, reimbursement policies may affect the procedural indications. In Japan, public health insurance covers all treatment costs, even for TAVR, resulting in the largest number of TAVR implants to date in Asia.[27] This implies that the generalizability of the developed AUC may be limited in other countries. Second, although the AUC has been designed to address many clinical scenarios commonly encountered in daily practice, it would be impossible to include every conceivable patient presentation. In the process of developing the AUC, only 6 factors that may affect the decision on whether to perform an intervention for AS and 8 factors that may affect the decision on the mode of intervention were considered; therefore, many relevant factors may have been unaccounted for. For instance, a hybrid approach with CABG plus TAVR would be a reasonable strategy to treat patients with AS and coexistent coronary artery disease; however, such a clinical scenario was not considered in the present study. Finally, due to the small number of panelists, personal bias and preference may have affected the appropriate ratings.

CONCLUSIONS

Using the RAND-modified Delphi panel method, we developed an AUC for the management of AS which provides a practical guide for physicians regarding clinical situations commonly encountered in daily practice. It also elucidates scenarios deemed rarely appropriate which are a clinical challenge for TAVR. Further investigations are necessary to assess how these AUCs are used and to change AS management in clinical practice after their publication. We will periodically update the criteria as new data and experiences become available.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Because of accumulating evidence on TAVR, its use has been rapidly increasing. However, the topic remains controversial; therefore, the indication for TAVR significantly varies among physicians and institutions.

TRANSLATIONAL OUTLOOK: Using the RAND-modified Delphi panel method, we developed AUC for the management of AS which provides a practical guide for physicians on clinical situations commonly encountered in daily practice. It also explains scenarios deemed rarely appropriate which are a clinical challenge in TAVR. Further investigations are necessary to assess how these AUCs are used and to change AS management in clinical practice after their publication.

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